HUMAN HEALTH SCIENCE CHAPTER OF BIS (BROMOACETOXY)-2-BUTENE

EXECUTIVE SUMMARY

The major use of bis (bromoacetoxy)-2-butene is as a slimicide in the manufacture of paper. The registrant has a use on the label for the preservation of water-based coatings.However, the registrant does not presently market the chemical for this use. It is the Agency understanding that the registrant intends to keep this use on the label.

Bis (bromoacetoxy)-2-butene(BBAB) is used as a slimicide in the manufacture of paper and paperboard products that contact food. This use results in a potential dietary exposure of this chemical to humans. The registrant submitted a migration study for this chemical to the Food & Drug Administration in the 1960's. This migration study does not reflect the use of simulating solvents that are recommended in the present FDA Guidelines.

The EPA has not used the FDA model for calculating residues that could occur in food that has contacted paper manufactured using the slimicide, BBAB. The FDA model assumes that the majority of slimicide is lost in the water from the paper-making process. The FDA review of the BBAB slimicide use reported very low BBAB residues expected in food contacting BBAB-treated paper. The EPA has also reviewed a 1960s BBAB migration study that does show migration of BBAB residues into food simulating solvents.

Consequently, the EPA has used a worst case calculation for estimating the level of BBAB that may migrate from BBAB-treated paper into food through contact with the treated paper. The EPA calculations assume that all of the BBAB used in the paper-making use ends up in the manufactured paper and that all of the residue in the paper migrates to food that contacts the paper.

HUMAN HEALTH ASSESSMENT OF THE CHEMICAL BIS (BROMOACETOXY)-2-BUTENE

Human Health Assessment

1. Exposure and Risk Assessment

a. Dietary Exposure and Risk Assessment

Bis (bromoacetoxy)-2-butene has a food use from its use in the manufacture of paper and paperboard that contact food. FDA has approved this use and the Regulation is codified 21 CFR 176.300 Slimacides. The Regulation states that the quantity added is not to exceed the amount necessary to accomplish the intended effect. The registered Slimacide V-10 label permits the application rate of 0.15-0.30 lb. of product(0.24 lb. active) per ton of paper produced.

Bis (bromoacetoxy)-2-butene also has a use for the preservation of water based coatings on the Busan 1210/Slimacide V-10 labels. The use of BBAB in paint is a treated article use as defined under 40 CFR 152.25(a) and is exempt from registration under FIFRA. The EPA considers that there is no dietary exposure from this use.

The coating use on the label is not being considered as a food-contact paper coating use because the label does not explicitly indicate that the coating use applies to paper; the EPA considers that the label use for paper is as a slimcide wet-end paper use and not a paper coating use. The label could be clarified to exclude the use of the product as a preservative for food-contact paper coatings.

i. Incidental Residues in Food From Treated Paper.

Worst Case Calculation for Residues in Food.

The FDA calculates residues in paper resulting from a slimicide use by using a model to calculate residues that will likely occur in paper. This model is not included in the "RECOMMENDATIONS FOR CHEMISTRY DATA FOR INDIRECT FOOD ADDITIVE PETITIONS". This model assumes that a large part of the slimicide chemical is "lost" in the water portion of the paper slurry in the paper-making process. After using the model for calculating residues in paper and in the absence of a migration study for residues

migrating to food, the FDA uses the Guidelines noted above for calculating residues in food. The worst case calculation for migration of BBAB residues from treated paper to food assumes that 100% of the BBAB paper additive migrates to food from the treated paper.

The FDA "model" for calculating residues that will result in paper was not used for this BBAB slimicide use because that model assumes that a significant part of the slimicide is "lost" in the paper manufacture with the water from the paper slurry. In this case, BBAB residues are not water soluble and could preferentially stay with the paper pulp and would not be carried away with the water from the paper slurry. Furthermore, there is a BBAB paper migration study(discussed below). This study, however, is over thirty years old and does not follow present FDA guidance for conducting a migration study. The study does show that detectable BBAB residues are present in the manufactured paper and are extracted into the food-simulating solvents used in the migration study. Consequently, there is the possibility that BBAB residues will occur in the diet. For this reason, the FDA model for calculating residues in paper was not used in calculating the dietary exposure for BBAB from this use.

Instead of using the FDA model for calculating residues in paper from the slimicide application for the reasons stated above, it was assumed here that all of the BBAB chemical that was added to the paper-making process was concentrated in the finished paper. The FDA guidelines for calculating exposure as described in "RECOMMENDATIONS FOR CHEMISTRY DATA FOR INDIRECT FOOD ADDITIVE PETITIONS" for calculating residues in food were then used in calculating residues in food.

The assumption was made that the basis weight of a treated paper is 50 pounds/3000 square feet or 50 milligrams/square inch. This is the example used in the FDA guidance document. (Note: Papers with various weight bases will be treated with the BBAB additive.)

Both the FDA method of calculating residues expected in paper and food and the method used by EPA for BBAB will be calculated below.

FDA Method

Using this assumption, the maximum weight of BBAB per unit area of paper as calculated by FDA is:

Given: The label allows 0.30 lbs. of 80% product per ton of paper or 0.24 lbs. of active) per ton of paper of paper fiber.

The FDA assumes that paper pulp is about 0.6% of the paper slurry(the water paper pulp mixture). 2000 lbs. paper pulp/0.006(the percentage of paper pulp in the slurry) = 333,333 lbs. of slurry.

Then 0.24 lbs. active/333,333 lbs. of slurry = 0.72 ppm of BBAB in the paper slurry.

Then the concentration of active ingredient (a.i.) in the pulp prior to entering the driers is:

(application rate) x (water/pulp ratio)

0.72µg. of paper slurry) x 0.67 gm. water/0.33 gm. pulp = 1.5 µg. a.i./gm. pulp

Then the dietary concentration is:

(µg. of a.i./gm. of pulp) (gm. of pulp/gm. of paper) (basis weight of paper) (food mass to surface area)

(1.5 µg. a.i./gm. pulp) (0.92 gm. pulp/gm. of paper) (0.05 gm./in.^{2}) (1 in.^{2}/10 gm. food) = 0.0069 µg. of a.i./gm. food.

Using a Consumption Factor of 0.1(from the FDA recommendations For Chemistry Data For Indirect Food Additive Petitions) for uncoated paper, the concentration of BBAB in the daily diet is then:

0.0069 µg. a.i./gm. of food x 0.1 = 0.00069 µg. of a.i./gm. of food.

Assume 3 kg. of food consumed/person/day, then:

3000 gm. of food x 0.00069µg. BBAB/gm. of food = 2.1 µg./person/day of BBAB.

EPA calculation

Given: The label allows 0.30 lbs. of 80% product per ton of paper(or 0.24 lbs. of active). This is equivalent to 120 ppm BBAB in the paper. Then:

120 x 10^{16}g(120) ppm/g of paper x 50 mg/in^2 = 0.006 mg BBAB/in^2.

If all of the BBAB additive in the paper migrates into food and 10 g of food is in contact with 1 square inch of paper (FDA usual assumption), then the maximum concentration of BBAB residue would be 0.600 ppm or 600 ppb.

0.00600 mg BBAB/10 g food = 0.600 ppm.

The estimated daily intake of BBAB for an individual would be as follows:

The FDA guidance "RECOMMENDATIONS FOR CHEMISTRY DATA FOR INDIRECT FOOD ADDITIVE PETITIONS", Appendix IV, Table I lists the consumption factor for uncoated paper as 0.1.

Then:

3000 gm. food/person/day(FDA assumption) x 0.600ppm x .1 = 0.18 mg BBAB or 180 µg intake/person/day.

As stated above, the EPA calculation did not use the FDA model because BBAB is not water soluble and also because the results of an earlier migration study conducted in the1960s did show a BBAB migration of residues into food simulating solvents.

Estimate of Residue in Food Based on Submitted Data.

The data submitted to the FDA to support the BBAB use in the manufacture of paper and paperboard that contacts food is a study that was conducted in 1960 entitled, "Migration of Vineland V-10 Germicide Into Food Simulating Solvent". In that study, various types of paper were manufactured using different dosage rates of BBAB in the manufacturing process. The paper types included wax bakery tissue, freezewrap, steak interleaving paper, bubble gum box and specialty food board. The study was modeled after FDA data requirements at the time the study was conducted. The study design and food simulating solvents are not the same as those recommended in the present FDA recommendations.

The present FDA recommendations assume 10 g of food contact each square inch of surface area. The present FDA guidance document also recommends that a migration study be conducted using either a particular type of packaging or with the use of a migration cell. For this study, the petitioner did not use 10 ml of simulating food solvent for extraction purposes. Instead, 2 ml of food solvent contacted each square inch of paper in this study. Adjusting for volume, 10 ml of food solvent would contain 20% of the BBAB migrant concentration that 2 ml of food simulating solvent would contain. Furthermore, the BBAB application rate in the paper manufacture in this study was lower than that now registered for use. Hence, the residue levels extracted into the food simulating solvents have been adjusted for application rate in the EPA calculations.

Therefore, the concentration of BBAB additive in the food simulating solvents was adjusted for the application rates now registered for use in the paper manufacture and further adjusted for the 2 ml/square inch food solvent used in the study.

The analytical method used to generate the residue data in this 1960 study was a colorimetric method. In this method, the BBAB is hydrolyzed with sodium hydroxide to yield bromide. The bromide ion is then converted to bromate with hypochlorite solution. The bromate is quantitatively reacted with sodium bromide to yield bromine which is then reacted with rosaniline to produce a red color. The intensity of the color is proportional to the amount of bromate. The absorbance is measured at 570 millimicrons with a photometer.

The concentration of BBAB in the food contacting the steak interleaving paper is 0.32 ppm. This paper had the highest residue in the 1960 study submitted to the FDA. The concentration of BBAB in the daily diet from the use of BBAB in paper manufacture is 0.032 ppm.

The estimated daily intake of BBAB, assuming no other dietary sources of BBAB is 0.1 mg.(100 µg.). This assumes a daily intake of 3 kg of food/person/day.

Note: Treated paperboard was also used in this study. For a paperboard product, the basis weight of the paperboard would be much higher, e.g. 300 mg/in^2. This would result in a much higher concentration of BBAB/square inch in the paperboard manufacture. However, the experimental data from this study showed no extraction of BBAB from the paperboard product. Therefore, the treated steak interleaving paper data were used for this RED because it provided a worst case situation.

Because the study does not follow the FDA recommendations for conducting this type of study and because of the calculation adjustments made to the data from this 1960 study, it is recommended that the worst case calculation be used for dietary risk assessment rather than the 1960 study. The paper and paperboard manufacturing use for BBAB appear to be the only use for BBAB with a dietary impact.

The worst case calculation for estimated daily intake of BBAB/person is 0.18 mg or 180 µg.

REFERENCE

1. MIGRATION OF VINELAND V-10 GERMICIDE INTO FOOD SIMULATING SOLVENTS. Microbiological And Biochemical Center Syracuse University Research Corporation. March 3, 1960. Revised April 1963.